REMARKS

This amendment and these remarks are responsive to the Office action dated August 8, 2006. By way of this amendment, claims 1-25 and 30-35 are currently pending, claims 26-29 and 36-102 have been cancelled without prejudice and new claims 103-148 have been added.

Specification:

In the Office action, the title is objected to for not being descriptive. Applicant has amended the title to METHODS FOR COVALENTLY ATTACHING POLYPEPTIDES TO SUBSTRATES as suggested by the Examiner.

Claims:

In the Office action, claim 37 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "said thiolate diazonium group" without proper antecedent basis. By way of the present amendment, claim 37 has been cancelled without prejudice. Accordingly, Applicant believes this rejection is moot.

Claims 1, 19, 30 and 32 were rejected under 35 U.S.C. 102(b) as being anticipated by Curreli et al. In order to anticipate a claim, a reference must teach each and every limitation of the claim. As amended, claim 1 recites an inorganic siloxy amine treated substrate. The only substrate disclosed in Curreli is Poly (vinyl alcohol), which is an organic substrate. There is no discussion of the use of any other substrates, or the siloxy-amine treatment. Accordingly, Curreli fails to teach an inorganic siloxy amine treated substrate.

Furthermore, claim 1, as amended, recites a polypeptide covalently bound to the diazotized tether group, wherein the polypeptide is bound to the diazotized tether group by an exogenous his-tag. While the Curreli reference discusses the binding of diazotized tether groups to endogenous histadine and histamine residues, the Curreli reference makes no mention of the possibility of binding of proteins via exogenous his-tags.

Accordingly, for at least these reasons Applicant respectfully submits that claim 1 is not anticipated by Curreli. Moreover, because claims 19, 30, and 32 depend from claim 1 and therefore include all the limitations of claim 1, Applicant respectfully submits that these claims are not anticipated by Curreli for at least the same reasons.

Claims 1, 19, 30-33 and 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark. Claims 36 and 37 have been cancelled without prejudice by way of this amendment, accordingly, the rejection of these claims is moot. As amended, claim 1 recites an inorganic siloxy amine treated substrate. Like Curreli, Clark teaches only organic substrates such as polystyrene. There is no discussion of the use of any other substrates, or the siloxy-amine treatment. Accordingly, Clark fails to teach an inorganic siloxy amine treated substrate. Moreover, as discussed by the Examiner in the Office action, Clark fails to teach attachment of a polypeptide to a diazotized tether group via a his-tag. Accordingly, applicant respectfully submits that claim 1 is not anticipated by Clark. Because claims 19 and 30-33 depend from claim 1, Applicant respectfully submits that these claims are not anticipated by Curreli for at least the same reasons.

Claims 2-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark

in view of Fancy et al and/or Curreli et al. In order to establish a *prima facie* case of obviousness there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the referenced teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed, Cir, 1991), see also MPEP 2142. Moreover, the mere fact that the references can be combined does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990), see also MPEP 2143.01.

The failings of Clark and Curelli with respect to amended claim 1 (from which claims 2-8 depend) are disclosed above. Specifically, Clark and Curelli fail to teach or make obvious an inorganic siloxy amine treated substrate and attachment of a polypeptide to a diazotized tether group via an exogenous his-tag. Fancy similarly fails to teach or make obvious an inorganic siloxy amine treated substrated and attachment of a polypeptide to *a diazotized tether group* via an exogenous his-tag. Instead, the his-tag described in Fancy is used to deliver a nickel-based crosslinking reagent to the tagged proteins. (See e.g. pg. 551, "Results" and throughout).

Accordingly, because none of the cited references disclose or make obvious an inorganic siloxy amine treated substrate and attachment of a polypeptide to a diazotized tether group via an exogenous his-tag, as recited by claim 1, from which claims 2-8

depend, Applicant respectfully submits that the Examiner has failed to establish a prima facie case of obviousness with respect to claim 2-8.

Moreover, Applicant respectfully submits that it would not be obvious to modify the teachings of Clark, Curreli, and Fancy, to produce applicant's claimed invention, because the Clark, Curreli, and Fancy papers all refer exclusively to organic substrates. Applicant respectfully submits that it is well known in the art that the specific coupling-chemistry that is used for organic substrates will not work for inorganic substrates. Accordingly, even if it were obvious to modify the cited references for use with an inorganic substrate, there would be no expectation of success. Furthermore, Applicant respectfully submits that absent knowledge gleaned from Applicant's present disclosure, due to the well-known highly fickle nature of polypeptide-binding chemistry, it would not have been obvious that a diazotized siloxy amine treated inorganic substrate would be a suitable platform for attachment of his-tagged polypeptides.

Extrinsic evidence of the non-obviousness of the presently claimed invention is further available. Specifically, a paper authored by a number of the present inventors describing the presently claimed invention was published this year in the journal Bioconjugate Chemistry, which is published by the American Chemical Society. See, e.g. Wu, Yang, et al., "Diazo Coupling Method for Covalent Attachment of Proteins to Solid Substrates" Bioconjugate Chem. 2006, 17, 359-365. It is noted that this paper was found to be worthy of publication a full 10 years after the Fancy paper published and the Clark patent issued and a full 9 years after the Curreli paper published. Accordingly,

Applicant respectfully submits that, as evidenced by the recent publication of the above-referenced paper, the presently claimed invention has been determined to be novel and non-obvious by Applicant's peers in the industry.

As an aside, it is noted that the Examiner has made reference to the Curreli paper at page 1437, first full paragraph, as providing evidence regarding the possible location of the histadine residue in the immobilized protein. Because applicant does not wish to be construed as having acceded to points which Applicant does not believe are, in fact, made by any cited reference, Applicant respectfully points out that the paragraph cited by the Examiner refers only to the determination of whether or not a *tyrosine* residue could conceivably be present within the active site of glycanases and glycosidases, potentially leading to enzyme inactivation. No mention is made in the paragraph of histadine residues.

Claims 9-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark in view of Fancy et al and Curreli et al. By way of the present amendment, claims 9-15 have been cancelled without prejudice, thereby mooting the rejection.

Claims 16-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark in view of Blackburn. By way of the present amendment, claims 26-29 have been cancelled without prejudice, thereby mooting their rejection. In the Office action, the Examiner states that Clark fails to teach the claimed substrates, and Applicant agrees. The additional failings of Clark with respect to claim 1, from which claims 16-29 depend are discussed above. Applicant respectfully submits that Blackburn similarly fails to

teach or render obvious a siloxy amine treated substrate and/or a polypeptide bound to the diazotized tether group by an exogenous his-tag. Accordingly, even if it were obvious to combine these references, applicant respectfully submits that the limitations of claims 16-29 are neither taught nor rendered obvious by the cited references. Furthermore, the extrinsic evidence regarding non-obviousness presented above is reiterated.

Claims 34-35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark. The failings of Clark with respect to claim 1, from which claims 34-35 and 37 depend are described above and relied upon here. Again, applicant respectfully submits that Clark fails to teach or render obvious each and every limitation of the presently rejected claims.

New claims:

New independent claim 103, from which new claims 104-126 depend, recites an inorganic siloxy amine treated substrate, a diazotized tether group bound to the substrate, and at least one polypeptide bound to the diazotized tether group by an exogenous tyrosine tag. Support for new claims 103-126 can be found in the claims as originally filed and throughout the specification. Support for tyrosine tags, as recited in the present claims, can be found, for example, in paragraph 77. No new matter has been added. As discussed above with respect to claim 1, Applicant respectfully submits that none of the cited references teach or render obvious an inorganic siloxy amine treated substrate. Furthermore, Applicant respectfully submits that none of the cited references teach or make obvious the binding of a polypeptide to a diazotized tether group by an exogenous

tyrosine tag. Applicant's arguments above with regard to additional extrinsic evidence of non-obviousness are again relied upon here.

New independent claim 127, from which new claims 128-148 depend, recites a microarray comprising an inorganic thiolate amine treated substrate, a diazotized tether group bound to the substrate, and at least one polypeptide covalently bound to the diazotized tether group, where the polypeptide is bound to the diazotized tether group by either an exogenous his-tag or an exogenous tyrosine tag. Support for new claims 127-148 can be found in the original claims as filed and throughout the specification, see e.g. paragraphs 15, 77, and throughout. No new matter is added. Applicant respectfully submits that none of the cited references teach or render obvious an inorganic thiolate amine treated substrate. Furthermore, Applicant respectfully submits that none of the cited references teach or make obvious the binding of a polypeptide to a diazotized tether group by an exogenous his or tyrosine tag. Applicant's arguments above with regard to additional extrinsic evidence of non-obviousness are again relied upon.

Conclusion:

Applicant believes that this application is now in condition for allowance, in view of the above amendments and remarks. Accordingly, applicant respectfully requests that the Examiner issue a Notice of Allowability covering the pending claims. If the Examiner has any questions, or if a telephone interview would in any way advance prosecution of the application, the Examiner is requested to please contact the undersigned attorney of record.

CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being to transmitted to the USPTO via secure EFS on December 7, 2006

Ellen Gonzales

Respectfully submitted,

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